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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/897,233	07/02/2001	Otto Schallner	Mo-6411/LcA 34,261	8201

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EXAMINER

HANLEY, SUSAN MARIE

ART UNIT	PAPER NUMBER
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1651

DATE MAILED: 12/14/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/897,233

Applicant(s)

SCHALLNER ET AL.

Examiner

Susan Hanley

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 21 September 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-10,23,26-31 and 36 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-10,23,26-31 and 36 is/are rejected.
- 7) ☒ Claim(s) 1,2,23,10,31 and 36 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 02 July 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
- 1) ☒ Certified copies of the priority documents have been received.
 - 2) ☐ Certified copies of the priority documents have been received in Application No. _____.
 - 3) ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date 6/18/02.
- 4) ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election without traverse of group I, claims 1-10, 23, 26-31 and 36 in the reply filed on 9/21/04 is acknowledged.

Claim Objections

Claims 10 and 31 are objected to because of the following informalities: The terms "linker" and "substance" appear in quotation marks. It is suggested that the quotation marks be deleted because they could be mistaken for a printing correction symbol. Appropriate correction is required.

Claims 1, 2, 23 and 36 are objected to because the phrase "the anisotropy polarization values" is redundant. One of ordinary skill in the art would recognize that the phrase is synonymous with "the fluorescence polarization values." It is suggested that the phrase be deleted.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-10, 23, 26-31 and 36 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an assay for finding substances or evaluating if a substance binds to PPO by fluorescence polarization (FP) or anisotropy, does not reasonably provide enablement for an assay for finding substances or evaluating if a substance interacts to PPO by fluorescence polarization (FP) or anisotropy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make or use the invention commensurate in scope with these claims.

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Claims 1 and 2 are drawn to an assay for finding substances or evaluating if a substance interacts to PPO by fluorescence polarization (FP) or anisotropy. The specification discloses that the assays are based on the binding of a substance to PPO to form a conjugate which is detected by FP or anisotropy (p. 6). However, there is no disclosure related to an assay for finding substances or evaluating if a substance interacts in any possible manner with PPO and subsequently detecting such an interaction by FP or anisotropy. Moreover, the specification does not convincingly demonstrate how the skilled artisan would carry out an assay for determining if a substance has any possible type of interaction with PPO that can be determined by FP or anisotropy.

The limited showing of just two assays to detect a binding interaction between PPO and a substance is not sufficient to enable a claim drawn to an assay for determining if a substance has any possible type of interaction with PPO that can be determined by FP or anisotropy because the art of biochemistry is too unpredictable. One cannot assume that the ability of FP or anisotropy to detect binding between PPO and a substance ensures that FP or anisotropy can detect any manner of interactions between PPO and a substance with the same characteristics or capabilities. The instance specification does not define the term "interaction". Therefore it will be given its broadest reasonable interpretation which "to act on each other" (*Webster's Dictionary* p. 635). In a chemical sense, interaction can include binding to form a conjugate, reacting, electrostatic attraction or repulsion, magnetic attraction or repulsion, van der Waal's interaction, and so on. FP relies on the observation of the light emitted by fluorescently labeled molecules when they are in contact with another body, usually a protein or DNA. Thus, FP can detect binding interactions and depends on close contact of the two bodies to achieve any change in polarization (Chechovich, 1995). A compound having a magnetic property could interact with a protein at some distance without binding. Since, FP operates on the binding phenomenon, it would require undue experimentation for one of skill in the art to determine a magnetic interaction between PPO and a magnetic body.

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Thus, specification supports an assay to determine binding interactions between PPO and a substance by FP. However, the specification provides limited guidance for determining any possible interaction between PPO and a substance by FP. Considering the relatively high degree of unpredictability in the art of Enzymology, the specification does not enable one of skill in the art for an assay for finding substances or evaluating if a substance interacts to PPO by fluorescence polarization (FP) with undue experimentation. Thus, claims 1-10 are not commensurate in scope with the enabling disclosure.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-10 and 26-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is rejected because it is confusing. The stated purpose of the claim is to find substances which interact with PPO. However, the first step of the assay is drawn to preparing a mixture that already comprises a fluorescent substance that is capable of interacting with PPO. It is unclear what the purpose of the fluorescent substance. The phrase "preparing mixtures which comprise, in various concentrations" is unclear. Does this phrase mean that the concentration of each component in every mixture is varied relative to the concentrations of the other components in the mixture or that the concentration of each mixture, as a whole, differs from the other mixtures?

Regarding claims 10 and 31, the phrase "in each case" renders the claim(s) indefinite because the claim(s) include(s) elements not actually disclosed (those encompassed by "in each case"), thereby rendering the scope of the claim(s) unascertainable. See MPEP § 2173.05(d).

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Claims 10 and 31 are rejected because the phrase "it being possible" is a conditional phrase and the claim does not indicate the conditions for determining when the hydrocarbon chain is to contain the hetero components.

Claims 23 and 36 part (b) are rejected because the phrase "the mixtures of plane-polarized light" is confusing. It is suggested that it be changed to "the mixtures with plane-polarized light".

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-10, 23, 26-31 and 36 are rejected under 35 U.S.C. 103(a) as being unpatentable over Birchfield et al. (Pesticide Biochem. Physiol. (1997) 57:36-43) in view of Birchfield et al. (Biochem. (1998) 37:6905-6100, will be referred to as Birchfield-2), Sanchez et al. (J. Agric. Food Chem. (1993) 41: 2215) and Ghoshal et al. (US 5,986,094) and in light of *Webster's Dictionary* (1994).

Birchfield et al. disclose the study of the action of light-dependent peroxidizing herbicides on maize PPO at a high-affinity binding specific binding site with tritiated N-aryltetrahydrophthalimide

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[3H]THP (abstract). Binding studies were carried out with a cell extract of maize that was further purified to obtain solubilized PPO (p. 38, middle of left column). Competitive binding experiments were carried out with a radioactive assay that employed [3H]-THP and fourteen herbicides. I_{50} concentrations were measured (p. 39, left column).

Birchfield et al. do not disclose a method of finding substances that interact with PPO by fluorescence polarization wherein a substance is labelled with a fluorescent dye such as fluorescein having the claimed substance-linker-fluorescein structure or having an assay system comprising the claimed mixtures, an irradiation device and another device to measure FP.

Sanchez et al. discloses a fluorescence polarization immunoassay to screen for the herbicide dichlorprop. The assay is based on the difference in fluorescence polarization between free and antibody-bound fluoresceinamine-labeled dichlorprop. Antibodies to the herbicide were produced by immunizing a rabbit with dichlorprop-bovine serum albumin conjugates. Sanchez et al. teach the construction of a standard curve wherein known concentration of unlabeled dichlorprop, fluorescently labelled dichlorprop and antibody were incubated. The competition between the unlabeled DC and the labelled DC for the binding sites on the antibody allowed for the construction of a standard curve which describes the decrease in polarization by increasing concentrations of pesticide (p. 2215, right column, 3rd paragraph). The standard curve was used to determine the concentration of DC in spiked samples. The method was compared to an ELISA assay using the same set of reagents. The correlation was greater than 0.999 (p. 2219, 1st paragraph of left column). The specificity of the test was characterized by incubating the antibody and the labelled DC with structurally similar compounds that could compete with the labelled DC for the antibody binding sites. The concentration of each compound required to produce 50% inhibition of the fluorescence polarization caused by the binding of the antibody and the labeled DC was determined (p. 2218, 5th paragraph of left column and Fig. 4).

Birchfield-2 discloses the examination of the herbicide binding site of human of recombinant human PPO and the flavin cofactor using competitive radioligand binding experiments. Two

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radioligands were prepared from known PPO herbicidal inhibitors. The tritiated 5-azido analog of tetrahydrophthalimide ([³H]AzTHP) was employed. Birchfield et al. disclose that the tritiated diazoketone analog of acifluorfen, which is another PPO herbicide, has been employed in detecting yeast PPO. The binding of [³H]AzTHP to PPO was tested by introducing other known herbicides of PPP to compete with the radiolabeled ligand for binding sites on PPO.

Ghoshal et al. disclose the conjugation of 4'-methyl fluorescein derivatives to ligands via cyclic linkers to serve as fluorescent binding substances for FP assays. In Fig. 5, Ghoshal et al. teach how to reduce an aromatic nitro group to an aromatic amine which can then be attached to a linker that includes a cyclic group that is ultimately conjugated to the fluorescein derivative. Ghoshal et al. report that the synthesized fluorescent substances were employed to determine the amount of acetaminophen in serum or plasma samples.

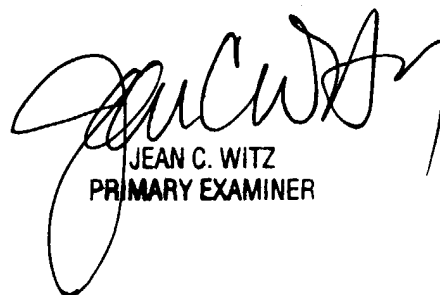
It would have been obvious to carry out the study of the binding of a PPO with other substances by FP that utilized an inhibitor of PPO conjugated to fluorescein and to make an assay system of the reagents and necessary instruments. Birchfield et al. teaches a radiolabeled binding assay for plant PPO. The ordinary artisan would have been motivated to employ an FP assay instead of one that uses radioactive reagents because radioactive materials are dangerous and require special care for storage (usually a special freezer), manipulation (depending on the type of radioactivity, the user must use a shield and take care to avoid excessive exposure) and disposal of waste (there are numerous regulations regarding the discard of radioactive substances). Thus, the ordinary artisan would have seen that using FP and fluorescent substrates would avoid all of these well known complications. The ordinary artisan would have had a reasonable expectation of success that PPO could be assayed by FP because numerous inhibitors bind to PPO and it is just a question of derivatization with a fluorescent compound. Ghoshal et al. demonstrated that the chemistry for modifying a compound for FP is well worked out and they exemplified how an aromatic nitro group can be reduced to an amine and eventually conjugated to fluorescein. Birchfield (2) taught that acifluorfen is a herbicide with an aromatic nitro group that has been

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used in a tritiated form to study binding to PPO. The ordinary chemist would have realized that the derivation of the nitro group on acifluorfen and the subsequent attachment to fluorescein could easily be achieved based on the fact that Ghoshal et al. accomplished the same transformation on a closely related molecule.

The combined disclosures fall within the scope of the claimed assay system which is interpreted as a kit. According to *Webster's Dictionary*, a kit may be defined as: 1. a set of articles used for a particular purpose, 2. a set of parts or materials to be assembled, 3. a packaged set of related materials, or 4. a container for a kit (p. 667). During the course of carrying out a binding assay for PPO by FP, all of the reagents and instruments would necessarily be gathered and thus lead to the claimed assay system with is a set of articles used for a particular purpose.

No claim is allowed.



JEAN C. WITZ
PRIMARY EXAMINER

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Susan Hanley whose telephone number is 571-272-2508. The examiner can normally be reached on M-F 9:00-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 571-272-0926. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Susan Hanley
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AU 1651